Intrauterine Insemination (IUI) With Clomiphene Citrate and Letrozole

Southern Ontario Fertility Technologies

Introduction

Intrauterine insemination (IUI) is the deposition of sperm into the cavity of the uterus using a fine plastic catheter. It is also sometimes referred to as "sperm washing". It is the simplest of the reproductive technologies. Some of the other infertility treatments such as in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) have a higher profile. Because of its simplicity, intrauterine insemination is much more affordable, less invasive and may be more effective overall, than the more intensive technologies.

IUI is believed to double to triple **the chance of pregnancy** in a cycle over and above anything else that is being done. This is probably especially true if mild male factor infertility is present. It is also extremely important if hostile cervical mucous exists.

Theoretically, IUI increases the chance of pregnancy by increasing the number of sperm entering the uterine cavity. We believe that when semen is ejaculated into the vagina that only 3-5% of the motile sperm navigate the cervical mucous to enter the uterine cavity. When sperm are washed, we can usually recover 20-50% of the moving sperm and these can be placed in the uterine cavity, thus making ten times the number of sperm available at this level.

IUI places 10 X as many sperm in the uterine cavity as even the most enthusiastic intercourse!

The increased number of available sperm might not be the whole answer. Intrauterine insemination also involves detailed monitoring of the cycle using blood tests and ultrasound. Perhaps this precise monitoring also adds to the improved success. It also bypasses the cervical mucous.

Clomiphene citrate (Clomid, Serophene) is a pill. It has been used to promote ovulation and therefore pregnancy since 1963! It is believed to double the pregnancy rate per cycle and may be responsible for even greater improvements in women who are not ovulating. A detailed information sheet is available on clomiphene citrate.

Both IUI and clomiphene citrate double the pregnancy rate. IUI with clomiphene together may quadruple the baseline spontaneous pregnancy rate and therefore has become a standard infertility treatment.

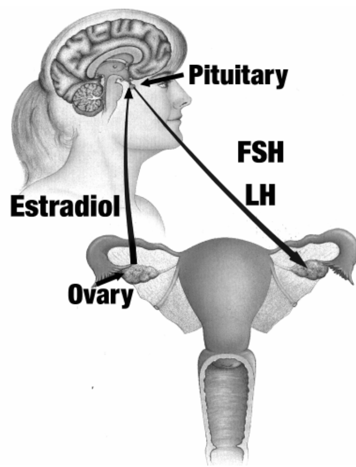
Who Can Benefit From IUI with Clomiphene Citrate

Most couples with infertility, as long as at least one fallopian tube is open and there are motile sperm in the males ejaculate can benefit from IUI. Once your infertility investigations have been completed, the type of treatment most suited to your circumstances can be determined. The decision to utilize IUI with clomiphene is made with your physician taking into consideration **the cause(s) of your infertility, length of infertility, female age, risks, benefits and cost**. This combination of technology is effective treatment for idiopathic infertility, anovulatory infertility, endometriosis-associated infertility, mild tubal-factor infertility and mild male-factor infertility. Many recent studies also support the use of IUI in female age related sub fertility. Usually, IUI with clomiphene is the next step if clomiphene with intercourse has not produced a pregnancy or may be used first if male-factor infertility is present.

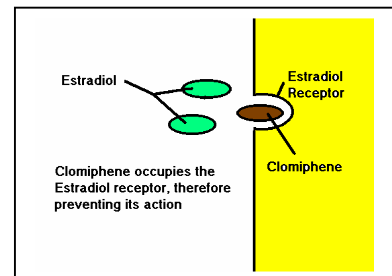
A Description of a Spontaneous or Clomiphene-Stimulated Cycle

The menstrual cycle is described in terms of days. **"Day one"** is the first day of vaginal bleeding requiring protection using more than a panty liner as long as it occurs before midnight. At this point most of the hormones are at very low levels. The cycle begins with **Follicle stimulating hormone (FSH)** being released by the pituitary and stimulating both egg-maturation and production of estrogen (estradiol). The estrogen stimulates the growth of the endometrial lining. In a successful (ovulatory) cycle, the combination of FSH and estrogen facilitates a rapid release of Luteinizing Hormone (LH). This rapid, high level of LH is often referred to as the **LH Surge** and is thought to induce final maturation and release of the egg (ovulation) about 34 to 36 hours after its peak.

How Clomiphene Works



Menstruation and ovulation are complex processes that depend on the action of hormones released from the ovary, pituitary and hypothalamus. An imbalance in the levels of these hormones can disturb normal ovulation and can contribute to infertility. As written before, **FSH** is released by the pituitary and stimulates both egg maturation and production of estrogen (estradiol). The estradiol "feeds back" to the pituitary to cause a decrease in the secretion of FSH. In a woman who is ovulating each month, the FSH and estradiol take turns turning off and on, much like the furnace and thermostat in your house. Clomiphene essentially works by fooling the body into thinking there is less **estrogen**. It does this because it has the same three-dimensional shape as estradiol. It occupies its receptor so that estradiol cannot occupy the receptor. Estrogen needs to fit into the receptor to work. Therefore the estrogen does not feed back to the pituitary and the production of FSH is not turned off and more FSH is produced. This results in more stimulation of the ovaries and usually results in ovulation in a woman who has not been ovulating or in the production of more than one egg in a woman who is already ovulating.



How Clomiphene Citrate is Taken

Clomiphene is taken from day 3 to 7 of the cycle the same as when it is prescribed with spontaneous intercourse. Some physicians will prescribe clomiphene from day 5 to 9. This is not wrong and probably makes very little difference. More details about clomiphene citrate are available in the clomiphene information sheet.

What is IUI?

Intrauterine insemination is the deposition of sperm into the cavity of the uterus using a fine plastic catheter at the time of ovulation. Before semen can be injected into the uterine cavity it must be "washed". **"Sperm washing"** and IUI are the same technology.

Washing the sperm is the process of separating the sperm from the rest of the seminal fluid that makes up 95% of the volume of the ejaculate. This is done in the lab. Unprepared semen cannot be placed in the uterine cavity as it contains many biologically active components such as prostaglandins. If these were placed directly into the uterine cavity, they would make the woman very ill. Several techniques are available and the one that produces the highest recovery of sperm will be chosen for you. At the end of the sperm wash, as many of the motile sperm as possible from the original sample are suspended in a salt and protein solution. This solution is formulated to resemble the fluid found in a woman's fallopian tube. This process is not covered by OHIP and you will be **charged $200.00.**

On the day of the insemination, the male partner must produce a semen sample. Masturbating into a sterile container does this. Most of the time, it is easier for the male to do this at home and bring the sample to the clinic. As you go through your monitoring, make sure if you want to do the sample at home that you have a bottle. If your sample is required the next day and you don't have a sample bottle, don't use a substitute bottle. Come to the clinic the next day to produce your sample. In situations of great distances or when there is concern about the sample, it should be produced at the clinic. A men's room is available for this purpose. **Any sample delivered to the lab must have your name on it.** Unfortunately if you forget to put your name on the bottle, we cannot process it.

Some controversy exists about producing the sample **at home or in the clinic**. In fact, some infertility units will insist that the sample is produced on-site rather than at home. However, it has been our experience that sperm recovery rates are slightly higher from samples produced at home as long as they are properly transported to the clinic. To properly transport a sample, the specimen container should be placed under your shirt, next to your bare skin, as soon as possible after it is produced. This keeps the sample at about body temperature or a little bit lower. Samples transported in this way are usually stable for hours although we do encourage you to deliver your sample to the clinic as quickly as possible. Sperm are very sensitive to temperatures even slightly above body temperature so transporting them in another method (heat packs, warm towels, on the dash board next to the car heater) can be disastrous!

The preparation of the sperm for insemination takes 2 hours. We will usually ask for the sample at 8 am and the insemination will be at 10 or 11 am. Once your sperm sample is in our lab, it is very stable. During the sperm wash and after preparation, it is kept in an incubator at just below body temperature. Except in very rare circumstances, (previously frozen sperm or in some male factor patients) the sample **will remain stable for hours** thus allowing convenient scheduling of the insemination.

When you insemination is done, you will be given some information about your sample. Sometimes all the numbers can be a little confusing!

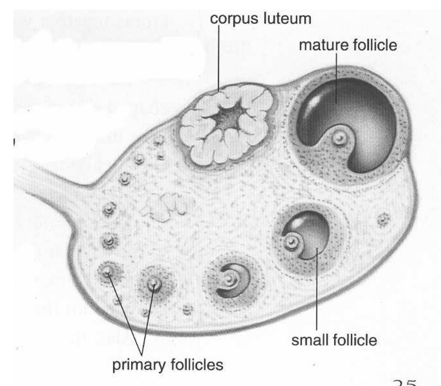
A basic semen analysis is always done on the sample. This includes the **volume** or amount of fluid, the **concentration** or number of sperm in each milliliter of ejaculate and the **motility** or percentage of the sperm that are moving. From these numbers we will calculate a **"total motile count"** which refers to how many moving sperm were in the original sample.

When your sample is washed we will calculate two more numbers. The first will be the **"total motile count" of the sample**. This is the number of moving sperm available for us to inseminate. This is the most important number for you as it determines (with other factors) the chance of a pregnancy from the insemination. (A discussion of this is available in the information sheet on male infertility) The last number we will tell you is the **percent recovery**. This is the percent of the moving sperm that are available for insemination compared to the moving sperm in the original sample. Usual sperm recoveries are 20%. Sperm recovery is not only based on our technique but as well on some characteristics of the sample. However, at S.O.F.T., we try very hard to get as many sperm for insemination as possible and our recoveries are often much higher.

Some controversy has existed in our medical literature about **the benefit of two inseminations as apposed to a single insemination**. In 2003, we completed a large study at S.O.F.T. to try to solve this question and we found some interesting results. In the next section of this information sheet the timing of the insemination and how we monitor you to determine exactly when to do you insemination is discussed. This is important to this discussion as it influences whether two inseminations will be helpful. Our findings were that two inseminations were most helpful when some male factor infertility is present and when the timing of the insemination is determined by the "LH surge" rather than an HCG injection. Male factor was deemed to be present if the total motile count of the insemination sample was less than 5 million sperm. The timing of the procedure and the benefit of two inseminations will be discussed in the next section. In general, we will suggest two inseminations instead of one if the first insemination contained fewer than 5 million sperm and your insemination was timed from a spontaneous LH surge. You will be charged $250.00 for a double insemination.

Timing the Procedure

The success of IUI depends on timing it with **ovulation or release of the egg from the ovary**. Ideally, the insemination should be done at the exact time when the egg or eggs are being released from the ovary. IUI cycles use **both blood tests and vaginal ultrasounds to determine when this occurs.**



The beginning of the cycle is referred to as "day 1". "Day 1" is the first day of menstrual bleeding requiring more than a panty liner for protection. All hormone levels are very low and the ovary should contain only very small follicles. Follicles are small cystic structures which contain the eggs and produce the ovarian hormones. We can figure out how the cycle is progressing by measuring the growth of the follicle(s) and measuring the blood level of key hormones.

The first thing that happens in the cycle is that the pituitary gland produces **follicle stimulating hormone (FSH)**. This causes a follicle, or in the case of a clomiphene-stimulated cycle, more that one follicle to grow in the ovaries. The follicle(s) produces **estrogen** in increasing levels as it grows. In most cycles the estrogen increases each day and we measure this increase during the critical time of the cycle. Another hormone, Luteinizing

hormone (LH) stays low during the first part of the cycle. However, once the estrogen reaches a certain level or a follicle becomes a certain size; a **LH surge** occurs (a doubling or tripling of the level). The LH surge is then used to time the insemination. In spontaneous cycles the LH surge usually occurs on day 12 or 13, however, in clomiphene-stimulated cycles, the LH surge is usually delayed until day 14 to 16. Once the LH surge has occurred the estradiol level usually drops. In fact, with our monitoring, we can determine if we are at the beginning or end of the LH surge by the estradiol level. If it is still rising, we are at the beginning of the LH surge; if it has dropped from the previous day, we are at the end. The peak of the LH surge occurs 34 to 36 hours before the release of the egg(s).

If a spontaneous LH surge is used to time your insemination, insemination will be done the day after the surge is detected (therefore about 10 hours, if it was the peak of the surge, before egg release). However, if your cycle requires an HCG injection to release the eggs, the injection should be given about 10 pm the night and the insemination will be the day after next (about 36 hours after the injection, therefore just about when the egg(s) are being released).

The dynamics of a cycle with clomiphene is presented in this table. **This table is an example only and individual cycles may vary widely.**

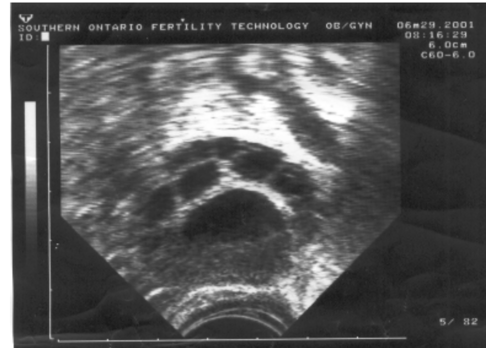
Cycle Day	Estradiol E_2	LH	Follicle Size (mm)
Day 1	50	4	2
Day 3	100	3	5
Day 6	200	4	8
Day 8	300	3	11
Day 10	450	4	14
Day 11	600	3	15
Day 12	750	6	17
Day 13	900	5	19
Day 14	1050	7	21
Day 15	1200	12	23
Day 16	1250	**75**	24
Day 17	850	20	24

Usually, blood tests (estradiol and LH) are performed daily from day 11 of the cycle. In the cycle, the estradiol should increase slowly and the LH should stay consistently low until one day it rises dramatically. The **"LH surge"** refers to a rapid release of luteinizing hormone from the pituitary gland before ovulation occurs and is reflected in the LH blood test by a doubling or tripling of the baseline level. The insemination is performed the day after the "LH surge". If the follicle(s) have grown to a good size (16 mm and over) or you get to day 16 of the cycle and a LH surge has not occurred, we will suggest **an HCG injection.** An HCG injection is an artificial LH surge. By using HCG we prevent extended monitoring of your cycle and cycles in which an egg or eggs are produced but not released. A LH surge does not always occur in cycles being monitored for IUI. This can happen even if there is normal egg development. In natural cycles this has been named "luteinized, unruptured follicle syndrome" and is thought by some to contribute to some infertility.

Unfortunately, the results of **the blood test required for this monitoring have to be available the same day**. This usually requires them to be done at S.O.F.T. We have been able to arrange same-day blood testing in some cities (IE Windsor, Kitchener and Sarnia). This can only be done on weekdays and on days that you don't have to have an ultrasound. If you are interested in doing some of your blood testing in these labs, you should speak to the nurse about it on your first day of monitoring. This is usually reliable, but S.O.F.T. cannot take responsibility for the result being sent to us the same day. This can make doing an IUI cycle very stressful and fatiguing. We try to make this less stressful by performing the

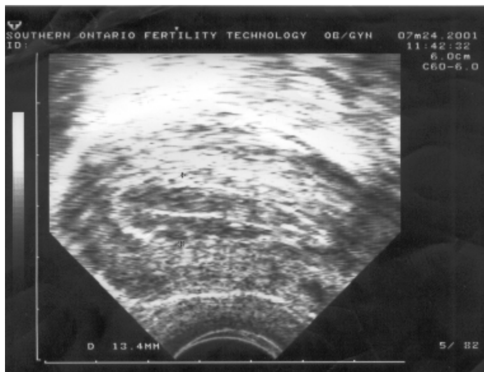
monitoring blood tests at the clinic (one stop shopping!). Also, instead of rigidly having to do the tests first thing in the morning, they can be done as late as 1 pm on most weekdays.

Blood testing, ultrasounds and inseminations may need to be performed 7 days a week at the clinic. For this purpose, S.O.F.T. is open from 7:30 am to 1 pm weekdays and 8:30 am to 10 am on weekends. On weekends and holidays only the back door of the building will be open.



Ultrasound of an ovary with many small follicles but one central follicle, which has become larger

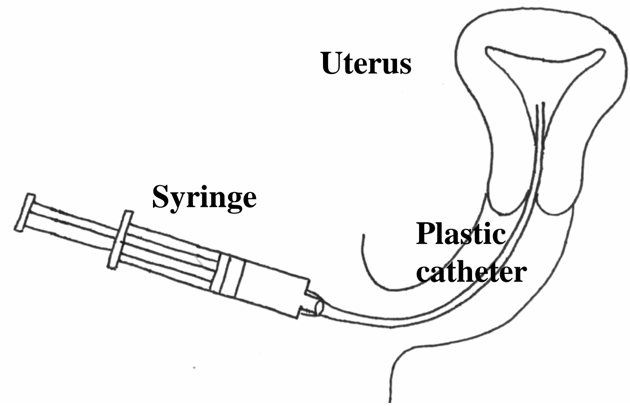
Vaginal ultrasound monitoring of IUI cycles is also be important. It is employed in clomiphene cycles on day 11 or 12 to determine how many potential eggs are developing and to ensure that the endometrium is of adequate thickness. (Vaginal estrogen may be prescribed if the lining is too thin.) Follicles that may go on to ovulate are usually 11 mm or more in diameter by your first monitoring day. If all follicles are smaller than this it may mean that you will not ovulate in this cycle. If the follicles are very large, it may mean that they are left over from the last clomiphene cycle or that you are going to ovulate earlier than usual in this cycle. Ultrasound is also important in cycles were a spontaneous LH surge does not occur and helps to determine when HCG should be given. In clomiphene cycles were a spontaneous LH surge does not occur by day 16 or sometimes earlier if the follicles are large, HCG (Profasi HP, Pregnyl) can be given to create an artificial LH surge. Follicles that are 16 mm or greater in diameter probably contain a mature egg. It used to be thought that if follicles got to large, they may not be good. However, we now know that even large follicles 30 to 34 mm can produce a pregnancy. When we decide exactly when to give HCG, the size of the follicles, the day of the cycle and the estradiol level are all taken into account. If you have a spontaneous LH surge, “Mother Nature” makes the decision for us.



Ultrasound of a uterus, which demonstrates a triple layer endometrium of adequate thickness

Whether your insemination is timed by an LH surge or HCG is also important as far as considering one or two inseminations. In our 2003 study, mentioned before, we found that the only group that statistically benefited from a double insemination was the group with male factor (less than 5 million to inseminate) and those whose insemination was timed by an LH surge. This makes some sense as with an LH surge, the insemination would occur before and after the release of the eggs. With HCG, the insemination would occur at the time of egg release and 24 hours after. The second one may than be too late.

The Procedure



Once the sperm washing is completed a small plastic catheter attached to a syringe is used to inject the sample. This is done in a clinic examining room. No preparation is required before the procedure is performed. Breakfast can be eaten normally and medication is not necessary before or during the procedure. You can drive yourself.

A speculum is placed in the vagina (similar to a Pap smear) and the catheter is fed up through the cervix (the opening to the uterus) and into the endometrial cavity. Once the tip of the catheter is in the endometrial cavity, the washed sample is injected. You are usually asked to remain lying down for 10 minutes after the catheter and speculum are removed. We will usually set a timer for you. You may then resume for full activities. As far as we know, there is no physical activity that makes it less likely for you to get pregnant. However, we do encourage you to make love in the next 24 hours as frequently as you can as this cannot possibly hurt and may be beneficial.

The semen sample has to be delivered to the clinic before the insemination (7:30-8 am on weekdays and 8:30-9 am on weekends and holidays (unless you are instructed differently) as the sperm washing procedure takes 2 hours. Inseminations are usually done between 10 am and 11 am but usually different times can be arranged if this is difficult for you to schedule.

Sample Safety

One of the most common worries of couples undergoing IUI is getting the wrong sample. **This is also of great concern to us at S.O.F.T. To ensure there is no mix-up of samples, we will never accept a sample that is not clearly labeled with your name.** During the processing of your sample, it never leaves a container that does not have your name clearly marked on it. All containers used are disposable sterile containers and a double check is made when the sample is transferred from one container to another. As we are preparing to do your insemination, you will be asked to check your name on the container.

Sexual Intercourse during Your Cycle

If we are using the male partner's sperm, we would like to inseminate with the greatest possible number of sperm. Sperm counts decrease if intercourse has occurred recently. Therefore we ask you to refrain from intercourse for one or two days before your insemination. This just means not to have intercourse after we have called to tell you that your LH surge has occurred. If HCG is ordered, do not have intercourse after it is given.

After the insemination has occurred we encourage you to have intercourse as often as possible over the next 24 hours. Ovulation has occurred and it seems logical to add as many sperm as possible. During other parts of the cycle, we encourage you to have intercourse as frequently as possible because it is good for your relationship and probably helps to maintain or increase the sperm count.

The Success Rate

IUI is very successful! The exact reason for this is not clear. It may involve the very careful monitoring to determine the time of ovulation, the bypassing of the cervical mucous and the placement of more sperm in the uterine cavity than would occur with intercourse or the fact that it is usually combined with medication to induce ovulation or produce more than one egg. An example will illustrate the effectiveness of IUI. A couple who have been trying to become pregnant for 2 years and have been investigated and found to have no apparent cause (idiopathic infertility) for their infertility have **a 2% chance per month** of getting pregnant. If that couple is given clomiphene and continues with intercourse their chance may increase to about **5% per month** for 6 to 12 months. However, if they participate in an IUI program combined with the clomiphene, their monthly chance rises **to 10 to 15%**. The pregnancy rate experienced with this treatment is remarkable considering many couples have already tried clomiphene citrate with intercourse.

10-15% doesn't seem very high but remember a 25 year old couple having intercourse at the time of ovulation has only a 15-25% chance each cycle

Because the success rate of IUI is only 10 to 15% per cycle, it **may take several cycles** to become pregnant. The average is 4 to 5 cycles. Up to six cycles (with any given protocol or medication) can be done before the chance per attempt decreases significantly. However, at the clinic, your cycle and overall treatment program is reviewed by the physician at the time of the insemination. Many times this will involve a discussion with you about your treatment options. Different medication protocols may be suggested before 6 cycles if the clomiphene is only producing one follicle, is thinning your endometruim, or for other reasons.

The usual next step, if clomiphene with IUI is not successful is to **increase or change the fertility medication** and continue with IUI**. IVF** (in vitro fertilization) or IVF with ICSI (intracytoplasmic sperm injection) may also be offered especially if a significant male factor is present. Sometimes **alternate medications** such as Tamoxifene or Letrozole will be suggested especially if you endometrium (lining of the uterus seems to be particularly sensitive to clomiphene).

Time and Expense

The decision to use IUI is usually only undertaken if the infertility diagnosis mandates it or when simpler therapies have been exhausted. When choosing clomiphene citrate with IUI, we have crossed the boarder between low-tech to **medium-tech treatment**. Monitoring is required to maximize the chance of pregnancy. This means daily blood testing from cycle day 11 or 12 until either a spontaneous LH surge has occurred or the decision to give HCG is made. Also at least one and usually more vaginal ultrasounds are usually done. Blood testing and vaginal ultrasounds are done at the S.O.F.T. clinic to minimize as much as possible the travelling and time commitments. However, for those living out of London, this can still involve many early mornings and a great deal of driving.

Clomiphene citrate should cost about **$35.00** if the lowest dose (50 mg X 5) is employed. If HCG is required for an artificial LH surge, it costs about **$90.00**. Many drug plans cover these but some do not. Be sure that your drug plan does not cover a certain number of cycles. If this is the case, you my be better to pay the drug costs for these cycles in case more expensive ones are required in the future. Additional expenses may include time

lost from work, transportation, and accommodation. The sperm washing is **$200.00**. There are no other hidden costs!

For your convenience, S.O.F.T. carries a supply of most of the drugs that we use for infertility treatment. These can be sold to you at our cost plus a very small handling charge with no dispensing fee. In most cases this will make them less expensive than from pharmacies. A receipt will be given for tax purposes or for reimbursement from your insurance company. Procedures or drugs can be paid for with VISA, Mastercard or Debit. The small "profit" we make on these drugs is used to keep other fees at a minimum. You can use your prepaid drug coverage for medications at any pharmacy. We often recommend Commissioners Pharmacy as it is close, works closely with us and is knowledgeable about our drugs and procedures.

Side Effects

The major side effect of clomiphene is an increase in the frequency of multiple births. **Twins occur in 5 to 10%** of these pregnancies but triplets are very, very rare.

Occasionally, abnormal temporary **enlargement of the ovaries** can occur. This usually is experienced as a feeling of mild bloating or pressure. Exaggerated enlargement of the ovaries is very rare and will respond to withdrawal of the drug for a cycle or two. In the past, patients on clomiphene required pelvic examinations between each cycle, but there is good evidence now that this is not necessary. Occasionally, when you are doing back-to-back cycles we will find a persistent follicle from your last cycle. This is not dangerous and will go away with time. Because the ovaries are working harder, you may experience a fullness or pressure in the pelvic area.

Hot flashes are the most common side effect while you are taking the drug. This occurs because clomiphene works by fooling the body into thinking there is less estrogen - less estrogen can simulate symptoms of menopause.

Other adverse reactions, occurring less frequently (1% or less of patients), include breast tenderness, headache, nervousness, dizziness, nausea and vomiting, fatigue and temporary visual disturbances.

Overall most women find clomiphene gives very few side effects and is easily tolerated. If you are experiencing many side effects or finding taking clomiphene unpleasant, please discuss this with us. If you have pain in the last half of a clomiphene cycle, please call the clinic and ask for a vaginal ultrasound.

IUI is extremely safe! I have never seen a very serious complication.

When the sperm are injected into the uterine cavity or as the catheter passes the narrowest part of the cervical canal, many women will experience **mild, short-duration cramping**. Sometimes, fluid will leak from the vagina right after the insemination is done. This is not the sperm coming out! One the sperm are in the uterus, they will not come out. The fluid is usually a combination of the warm tap water used to heat and lubricate the speculum and some vaginal secretions that come out when we open the vagina with a speculum.

Occasionally (less than 1 in 200-500 inseminations), a reaction will occur to the semen when it is placed in the uterine cavity. This usually consists of immediate pelvic cramping and some nausea. We believe this occurs because small amounts of "prostaglandins" remain with the sperm despite the washing process and is referred to as a

‘prostaglandin reaction”. Some women may also be more sensitive to small traces of these prostaglandins. If this reaction occurs it can be easily treated and steps can be taken with the next insemination to minimize the chance of recurrence.

Rarely (less than 1 in 10,000 inseminations), an **infection** can be introduced into the uterine cavity during the insemination. This will present as increasing pelvic pain in the day or two after the insemination. It is sometimes accompanied by a vaginal discharge, fever or chills. If any of these symptoms occur after an IUI, you should contact us or go to the nearest hospital emergency department. Prompt treatment will usually lead to an uneventful recovery.

Sometimes **spotting** will occur after the insemination. This happens because of an injury to a small blood vessel on the cervix at the time of the IUI. It will resolve by itself and does not decrease the chance of pregnancy.

Safety

Clomiphene citrate has been in clinical use since 1963. For most of that time it has functioned as the usual first step in fertility treatment except for couples with blocked fallopian tubes or severe male factor infertility. No one knows how many pregnancies have occurred using clomiphene but it is probably in the hundreds of thousands, if not in the millions. No clinical trial has ever demonstrated an increase in congenital abnormalities using clomiphene. Clomiphene does cause an increase in the twinning rate from 1.2% to 5%. Twins are a more difficult pregnancy and associated with more complication including prematurity.

IUI has never been associated with any increase in congenital abnormalities.

Initial Instructional Visit:

When we began the programs at S.O.F.T. we had you schedule a separate instructional visit to make sure you understood how everything worked. Now we will usually give you this information sheet before you start and answer any questions during your first cycle. We have found that by reading this instruction sheet, most patients are very informed about what they are doing. However, the staff is always happy to answer any of your questions and clear up any confusion. If you have a lot of questions, it is best to schedule a review visit with one of the doctors.

Also, during your first cycle, both you and your partner will have to do program blood work. Program blood work involves blood tests on both members of the couple, testing blood types, rubella status and for infectious diseases such as hepatitis and HIV. These tests are done for all couples doing IUI (or any other reproductive technology) and are mandated by our professional organizations. A uterine measurement (trial run of the insemination procedure) was done prior to your first insemination in the past. This is no longer done as it was found not to be helpful.

Injection of HCG:

As was discussed earlier in this instruction sheet, if a spontaneous LH surge does not occur but adequate sized follicles have developed, an injection of HCG will be ordered. You can inject this medicine and instructions will be given at the time that the injection is suggested for your cycle. An instruction sheet is available which describes the injecting technique in detail.

HCG injections are available in the clinic. Often during monitoring we will decide that if a spontaneous LH surge does not occur that day that you should take HCG. If you have not already filled a prescription for HCG we will send you home with the medication. If you do not need it, you can keep it for a few cycles and when you no longer require it (hopefully, you're your pregnant) you can bring it back. We will return your money minus a small restocking fee as long as it is not opened.

If you're IUI Cycle Doesn't Work???

Even if everything works well in your cycle, the chance of a pregnancy is still only 10 to 15%. Our overall pregnancy rate in all IUI cycles is 13.8%. Most of our research indicated that any given protocol in IUI maintains the same chance of pregnancy per cycle for 6 cycles. Therefore, if everything has been perfect, a repeat of the same cycle may be suggested if pregnancy does not occur.

Your cycle is evaluated at the time of your insemination. At that time changes in the medication for IUI, additional treatments such as laparoscopy, or moving on to another technology such as in vitro fertilization (IVF) may be suggested. Usually IUI will work for most patients. A common question that is asked after an IUI cycle that has not resulted in a pregnancy is: "Everything went so well – why didn't I get pregnant???" There are two basic reasons for this.

The first is that human beings are the most infertile species on earth! A couple in their 20's with no infertility factors will only get pregnant in 20 to 25% of their cycles. This % drops as they get older.

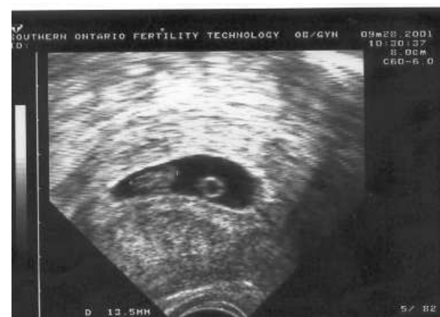
The second reason is that infertility diagnosis is extremely incomplete. We can test the basic hormones involved, make sure the tubes are open and count the sperm. We can even do laparoscopies and sperm function testing. However, there are so many other steps to getting pregnant that we cannot test.

Our basic approach to this is to eliminate as many of these unknown steps as possible and increase the number of chances. Therefore, the first treatment usually offered to couples is ovulation induction. This eliminates some of the unknowns as far as, "is ovulation fully occurring?" and usually provides more than one egg per cycle. The next step is usually IUI. This eliminates such steps as: "are sperm (and how many) getting through the cervical mucous?", "When is ovulation occurring?" and provides 10 X as many sperm at the endometrial level. The last step is usually the IVF process which takes many of those unknown steps out of the body and allows us to observe them.

At S.O.F.T., the decisions about your treatment will be made with you. You should never feel reluctant to ask questions or suggest things you have read about or found on the internet. We are always willing to discuss them with you and after all, you know your body best!

When you are Pregnant

After a positive pregnancy test, you will be asked to attend the clinic about 40 days after your insemination for a vaginal ultrasound. By this time we should be able to clearly see the gestational sac (bag of waters) inside the uterus, your baby and your baby's



Normal "luteal day 40" ultrasound of a single pregnancy

heart beating. A multiple pregnancy can also be diagnosed. It also is possible to diagnose problems with the pregnancy such as a miscarriage or ectopic pregnancies.

Although a perfectly normal ultrasound cannot guarantee a normal pregnancy because it cannot predict the future, it is very reassuring. Over 90% will go on to be normal pregnancies.

When the ultrasound is done, your due date will be calculated and a report will be sent back to your referring physician informing them of your pregnancy and asking them to take over your obstetrical care. After your ultrasound you are still considered our patient. Especially early in your pregnancy, if you have any concerns, perhaps because you have had bleeding or pain, we are more than happy to repeat your ultrasound. It is at this time we will also remind you of the **Clinic Rules**. Rule #1 is you have to send us a birth announcement and rule #2 is that you have to bring the baby to visit us.

Default Instructions:

Our clinic is run very efficiently but with a very small staff. We will do everything possible to facilitate your treatment and answer any of your questions. However, to make things run smoothly, we have developed "default instructions". This means that **unless we call you and tell you differently, the usual order of instructions should be followed.**

Below is a day-to-day description of an IUI cycle with clomiphene with the default instructions. Remember, this is the default. Your cycle may be very different and yet perfectly normal. For example, some patients will have large follicles on the first day of monitoring. Sometimes in this situation we will just suggest HCG the next day if a surge does not occur. Sometimes, the follicles will be very small on the first day of monitoring and we will advise you to take one or two days off before continuing the monitoring.

The day-to-day instructions will remain the same unless S.O.F.T. calls you with a change. The table indicates the default instructions. If an extra ultrasound is indicated, HCG should be given, a spontaneous LH surge has occurred or we want you to cancel your cycle, this will be discussed at your visit or we will telephone you. **If you do not get a telephone call or have not been instructed differently in the clinic, follow the table.**

For example, if you came for blood and ultrasound on day 11 and the largest follicle was only 12 mm, we would tell you to take a day off from monitoring because for an LH surge to occur you need a 16 mm or greater follicle. In contrast, if you came on day 12 and your follicles were all large (16 to 25 mm), we might ask for only blood work the next day and give you HCG if you didn't have the LH surge.

Cycle Monitoring – Day By Day (Default Instructions)

Cycle Day	Instructions	Patient Notes
Day 1	Call S.O.F.T. (519-685-5559) and inform us that your cycle has started The purpose of this call is not to make an appointment but to prompt us to make up a monitoring sheet for you. You will usually get the answering machine. Do not be alarmed – leave your message and tell us if you need anything else so we know to call you	

	back.	
Day 3	Baseline blood and/or vaginal ultrasound (Only if necessary – the default is none)	
Day 3-7 (5-9)	Take clomiphene citrate at the dosage prescribed.	
Day 11	Blood and ultrasound	
Day 12-15	Daily blood testing until LH surge Often we will ask for another ultrasound but the default is none	
Day 11 – 16	If an LH surge occurs (with good follicle(s)) insemination is scheduled the next day (you will be called)	
Day 16	Blood and ultrasound	
Day 16 or 17	If no LH surge and good size follicle(s), inject HCG (will be discussed at ultrasound)	
Insemination	Next day if LH surge detected Or if HCG is given at 10 pm - insemination will be the day after next (I,E,-36 hours) Double insemination in rare circumstances	
Semen sample	Samples should be delivered to the clinic at 8 am on weekdays and 8:30 on weekends and holidays You may be asked to produce your sample in the clinic (default is at home) **Your Name Must Be On the Sample Bottle**	
14 days after insemination	If no menses, a serum *B* HCG is done A repeat BHCG is requested in 48 hours if the first is positive.	
40 days after insemination	If pregnancy test positive, an early pregnancy vaginal ultrasound	

A Last Comment:

Any infertility treatment can be **frustrating!** We often refer to the emotional rollercoaster of infertility as hopes are increased by good responses to treatment, only to be dashed by a negative pregnancy test.

A 25-year-old couple having intercourse at the time of ovulation and having no infertility factors has only a 15 to 25% chance of a pregnancy. This makes humans' the most infertile species on earth!

The IUI program you have been referred to has a success rate of 10 to 15% per cycle of treatment. This is encouraging but **still leaves 85 to 90% of couples not pregnant each cycle**. If a cycle doesn't result in a pregnancy, this is disappointing **but doesn't mean that the treatment needs to be changed**. Most studies indicate that IUI with clomiphene remains equally effective for 6 cycles. Your treatment is constantly under review even if everything appears perfect. Usually, if you are not pregnant after 6 cycles it is time to

move on and more medication or a change of technology can be considered.

James Martin ©
S.O.F.T.
555 Southdale Rd. East,
London, ON, N6E 1A2
Tel: (519) 685-5559

Check out our web page at soft-infertility.com